

Allergic contact dermatitis from thiurams with pemphigus-like autoantibodies

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Case Report

A 42-year-old woman had undergone repeated reconstructive surgery of the lower limbs after a car accident. During rehabilitation, an emollient was applied daily on contracture scars. After 2 months, a severe erythematous-oedematous, vesicopustular, crusted reaction developed at skin donor and graft sites. A course of systemic antibiotics and topical corticosteroids was ineffective. Occlusive dressings of the lower legs with zinc paste bandages resulted in striking localized amelioration, while the thighs kept worsening and new vesicopustular lesions developed on the arms and face. Despite repeated swabs, bacteriological cultures remained negative. Allergic contact dermatitis from the emollient was suspected, but patch testing with the SIDAPA standard series and the emollient as is showed a ++ reaction to thiuram mix only. Further investigation revealed that the patient's mother had been using latex gloves to apply first the emollient and then the topical corticosteroids. Patch testing with the gloves elicited a discrete vesicopustular reaction at D2 and D3. Epidermolysis, reminiscent of Nikolsky sign, developed, close to the patch test site, upon removal of the Scanpor tape. During patch testing the eczema flared and spread to the trunk. Pruritus was intense.

Biopsy of a vesicopustular lesion from a thigh revealed subcorneal

blistering and eosinophilic spongiolysis. Direct immunofluorescence (DIF) was non-specific, showing only granular deposits of C3 at the dermoepidermal junction. Indirect immunofluorescence (IIF) demonstrated low titre (1/40) IgG autoantibodies to the intercellular substance. Weak serum positivity to desmoglein 1 and desmoglein 3 was found with ELISA. Western blot analysis was negative. Class II HLA-typing revealed the following haplotype: DR15, DR13, DR51, DR52, DQ1.

Strict rubber contact avoidance was advised and systemic prednisolone, 0.5 mg/kg daily was introduced. The dermatitis partly subsided, but relapsed when the drug was tapered and took on a chronic relapsing course.

Discussion

Our patient had developed sensitization to thiurams from contact with rubber gloves worn by her carer. This is a known, though infrequently reported, source of rubber sensitization (1). The clinical presentation was unusual: small vesicopustules, rapidly evolving into crusted lesions, were visible, both isolated and scattered on a background of florid eczema. During patch testing, a few epidermolytic lesions appeared at sites of skin trauma. Histological examination showed subcorneal blistering with eosinophilic spongiolysis and, in spite of negative DIF, pemphigus-like circulating autoantibodies were demonstrated by both IIF and ELISA. The clinical, histological and serological picture thus combined some features of allergic contact dermatitis with others of superficial pemphigus.

The onset and course of pemphigus is now held to depend on the interaction between endogenous (genetic and autoimmune) and exogenous triggering factors. The latter include drugs, physical agents, viral infections, dietary factors and contact dermatitis (2).

Drugs with sulphhydryl groups in their molecule (thiols) are particularly common inducers of pemphigus. They have been shown to cause direct acantholysis *in vitro*, by biochemical mechanisms interfering with the cyst-SH to cyst-SH bonds of

desmosomes, leading to loss of desmosomal function (3). In turn, alteration of the desmosomal structures may, *in vivo*, lead to the formation of neoantigens and the production of pemphigus autoantibodies.

Allyl compounds of garlic have also been shown to cause acantholysis *in vitro* and are suspected of contributing to the induction of pemphigus in patients who have pemphigus-prone antigens in their HLA haplotype (DR4, DR14) (4). Pemphigus can also be triggered by topical contact with exogenous chemicals ('contact pemphigus') and these cases often evolve from contact dermatitis into overt pemphigus (5–9).

In our case, contact with thiurams appears to have caused both allergic contact dermatitis and the production of specific pemphigus autoantibodies, with clinical signs of mild acantholysis.

We suggest that thiurams, acting like thiol drugs and garlic, may have induced direct superficial acantholysis. This, together with the allergic inflammatory reaction, may in turn have favoured the expression of desmosomal neoantigens, producing a specific autoantibody response. Overt pemphigus did not ensue, possibly because the patient's genetic background did not predispose her to it.

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